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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,067	12/28/2005	Gerd Sutter	GRUE-004	6100

24353 7590 06/23/2006

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER
HURT, SHARON L

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/532,067	SUTTER ET AL.	
	Examiner	Art Unit	
	Sharon Hurt	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *May 9, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments to the claims 1-17, received April 19, 2005 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 refers to the nucleic acid coding for the MSP-1 is reduced in its AT content compared to the wild type sequence. The specification does not define "AT" nor does it include examples of sequences for comparison of the "AT content". The claimed subject matter is not clearly defined for the instant invention. Claim 10 refers to the signal sequence controls the GPI anchoring of the gene product. . The specification does not define "GPI" therefore the claim does not particularly point out and distinctly claim the subject matter of the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that Aapplicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e. malarial proteins comprising the full length MSP-1, any fragments of the MSP-1, and any muteins of the MSP-1 incorporating any addition, any substitution, and/or any deletion of one or more amino acids.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.* the genus of malarial proteins comprising the full length MSP-1, any fragments of the MSP-1, and any muteins of the MSP-1 incorporating any addition, any substitution, and/or any deletion of one or more amino acids. The disclosure of even a single species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claims encompasses numerous species that are not described. There is substantial variability among these species. Applicant's disclosure is limited to the full-length MSP-

1 proteins and to the specific fragments designated p83, p30, p38, p33, p19, and p42. There is no disclosure of any of the other claimed fragments or muteins and no guidance as to where to make mutations in either the full-length protein or any of the recited fragments. In the absence of sufficient recitation of distinguishing characteristics of the species, the specification does not provide adequate written description of the claimed genus, which encompasses a myriad of muteins and fragments in addition to the full-length proteins.

One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (see *Vas-Cath* at page 1116).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-4, 6-7 and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al. (Vaccine, 1997, Vol. 15, No. 12/13, p. 1303-1313).

The claimed invention is drawn to a recombinant Modified Vaccinia Vaccine Ankara (MVA) virus comprising at least one nucleic acid coding for a *Plasmodium falciparum* merozoite surface protein-1 (MSP-1) protein or fragment or mutein, wherein the fragment is p83, p30, p38, p33, p19 or p42, wherein the mutein is differentiated from the MSP-1 sequence by addition, deletion, insertion, inversion and/or substitution of one or more amino acids, wherein the nucleic acid coding for MSP-1 is under the control of a promoter, wherein the nucleic acid at the 5' end is fused with a nucleotide sequence coding for a signal peptide sequence, wherein the signal sequence controls the GPI anchoring of the gene product. The claimed invention also is drawn to a method of production of the recombinant MVA virus comprising the steps: (a) transfecting a eukaryotic host cell with a transfer vector, wherein the transfer vector comprises a nucleic acid encoding a *Plasmodium falciparum* merozoite surface protein-1 (MSP-1) protein or a fragment or a mutein, wherein the mutein differs by the addition, deletion, insertion, inversion and/or substitution of one or more amino acids from the MSP-1 sequence, wherein the nucleic acid is flanked by MVA sequences 5' and/or 3'. Wherein the sequences are suitable for the homolgous recombination in the host cell; (b) infection with a virus based on MVA, preferably MVA; (c) cultivation of the host cell under conditions suitable for homologous recombination; and (d) isolation of the recombinant virus based on MVA, wherein the virus is isolated from the culture supernatant or from the cultivated host cells. The claimed invention is also drawn to a vaccine comprising the recombinant MVA virus and a pharmacologically compatible carrier, wherein the vaccine further comprises a MSP-1 fragment or a mutein and/or a

nucleic acid coding for MSP-1, or a fragment or mutein, wherein the constituents can be administered simultaneously, sequentially or separate. The claimed invention is also drawn to a method for the prophylaxis and/or therapy of malaria comprising administering the recombinant virus, MSP-1, a fragment or a mutein and/or a nucleic acid coding for MSP-1, or a fragment or mutein.

Yang et al. teaches a recombinant vaccinia virus encoding a *Plasmodium falciparum* merozoite surface antigen (MSA1) (p. 1303, Abstract). A highly attenuated strain of vaccinia virus, Modified Vaccinia Ankara (MVA) was developed as an expression vector and shown to be equivalent to replication competent vaccinia virus in several vaccine models (p. 1311, last paragraph). The merozoite surface complex is processed into fragments, 30, 38 and 42 k Da (p. 1304, top of left column). Each gene was inserted into the thymidine kinase region of the vaccinia virus, under the control of the synthetic strong early/late promoter (p. 1303, Abstract). The effect of signal and anchor sequence on the biochemical processing and antibody response to the C-terminus region of the MSA1 is expressed by recombinant vaccinia virus (p. 1304, left column). BSC-1 cells, a eukaryotic host cell, was transfected with a transfer vector, a recombinant vaccinia virus which encodes a *Plasmodium falciparum* MSA1 (p. 1305, left column). Insertion of the sequence, under transcriptional control of the promoter, provides a visual marker for identification (p. 1304, last pagragraph). The MSA1 fragments contain the 108 bp region directly downstream from the signal sequence and an additional 2 bp on the 5' end of the C-terminal to preserve the reading frame (p. 1305, Table 1). The vaccinia virus thymidine kinase sequences flanking the vaccinia

genome (p. 1304, last pagragraph). The virus containing the MSA1 was determined by SDS gel electophoresis from the cell pellets and 50X concentrated supernatants (p. 1308, left column). Yang teaches a vaccine composition complete with Freund's adjuvant administered to monkeys, mice and rabbits in one vaccine or in two parts (p. 1304, left column and p. 1307, left column). The vaccines were administered to mice for the prophylaxis of malaria with the recombinant vaccinia virus vaccine (p. 1308, right column).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and 6-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (Vaccine, 1997, Vol. 15, No. 12/13, p. 1303-1313) and McConkey et al. (Nature Medicine, June 2003, Vol. 9, No. 6, p. 729-735).

The claimed invention described above wherein the recombinant MVA virus coding for *Plasmodium falciparum* MSP-1 protein is of the isolate 3D7 or FCB1 strain,

wherein the signal peptide sequence controls the secretion of the gene product and the localization of the gene product relevant to the membrane.

Yang et al. does not teach the recombinant vaccinia virus MSP-1 protein is from the 3D7 or FCB1 isolate.

McConkey et al. teaches a recombinant MVA vaccine for protection against *Plasmodium falciparum* from the 3D7-strain (p. 729, Abstract and p. 731, last paragraph).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use MVA and the 3D7 strain of *Plasmodium falciparum* for the vaccine against malaria. The person of ordinary skill in the art would have been motivated to make that modification because this strain is well know in the art, and reasonably would have expected success because of the teachings of McConkey et al.

The following rejection is based on the judicial precedent following *In re Fitzgerald*, 205 USPQ 594 because the prior art is silent with regard to the signal peptide sequence controls: (i) the secretion of the gene product and (ii) the localization of the gene product relevant to the membrane. While Yang et al. does not particularly teach the two limitations described above, absent evidence to the contrary the signal peptide sequence controls would be expected to inherently perform the claimed process.

Under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art method. (MPEP 2112.02).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Yang et al. (Glycobiology, 1999, Vol. 9, No. 12, p. 1347-1356). Yang et al teaches a recombinant vaccinia virus that encodes the C-terminal portion of *Plasmodium falciparum* merozoite surface protein-1 (MSP-1), with or without an N-terminal signal peptide sequence and GPI signal sequence of MSP-1 (p. 1347, left column). Yang also teaches protein is cleaved into different sized N-terminal fragments (83, 28/30, 38 kDa) and a 42 kDa C-terminal fragment (p. 1347, right column).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Hurt whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

June 20, 2006

Brenda Brumback

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600